UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/977,137	10/12/2001	Anne O. Summers	79-00	2408

23713 7590 06/17/2003

GREENLEE WINNER AND SULLIVAN P C
5370 MANHATTAN CIRCLE
SUITE 201
BOULDER, CO 80303

EXAMINER
IBRAHIM, MEDINA AHMED

ART UNIT	PAPER NUMBER
1638	13

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/977,137	SUMMERS ET AL.	
	Examiner	Art Unit	
	Medina A Ibrahim	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *10-16* is/are withdrawn from consideration.

5)☒ Claim(s) *4* is/are allowed.

6)☒ Claim(s) *1,3,5,6 and 9* is/are rejected.

7)☒ Claim(s) *2,7 and 8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 May 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5 and 10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-16 are pending. Claims 15 and 16 are newly added.

Election/Restrictions

Newly submitted claim 15 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: A chelon protein having specified sequences. New claim 15 designated as Group III, and the invention of Group I are unrelated because the two inventions are directed to divergent molecules having different composition, structure, function, and effect. In addition, both the literature and sequence search of the two groups are divergent, and searching them together will pose serious search burden upon the Examiner. Therefore, the invention of Group III will not be grouped with Group I. (MPEP § 806.04, MPEP § 808.01). Newly submitted claim 16 is grouped with the invention of Group II.

I. Claims 1-9, drawn to a non-naturally occurring recombinant DNA molecule comprising a sequence encoding a chelon protein, a transformed host cell and a method for producing a recombinant chelon protein, classified in class 435, subclass 69.1, for example.

II. Claims 10-14 and 16, drawn to a method for removing a divalent mercury or cadmium by using a MerR or chelon protein, classified in class 800, subclass 278, for example.

III. Claim 15, drawn to a chelon protein, classified in class 530, subclass 323, for example

Applicant's election with traverses of Group I and SEQ ID NO: 4 in Paper No. 12 is acknowledged. The traversal is on the ground(s) that the restriction between the protein sequences of SEQ ID NO: 4-12 is improper because the sequences are related in both structure and function. Applicant argues that since the nucleotide sequences of the invention encode the chelon proteins of SEQ ID NO: 4-12 that differ in one or two amino acid positions, the restriction requirement should be treated as an election of species. Applicant also argues that new claim 15, drawn to chelon proteins should be grouped with the nucleotide sequences encoding them, host cells and methods of recombinant production of Group I. Applicant finally argues that, given the structural and functional relationship of the specifically exemplified chelon proteins, the utility of the DNA molecules, recombinant cells and methods of recombinantly producing the chelon proteins, in the method of removing metal ions, the invention of Group I and Group II should be examined together. Applicant requests withdrawal of the restriction requirement between Groups I and II, and requests that the election between SEQ ID NO: 4-12 be treated as election of species. These arguments have been considered but not all are persuasive.

Applicant's arguments that the restriction requirement between SEQ ID NO: 4-12 should be treated as elections of species are not found persuasive because sequences are considered to be patentably distinct inventions rather than species, since the structural variation between sequences is unobvious. However, since inventions (A)-(I) are synthetic variants comprising a common consensus sequence, the restriction

requirement between inventions (A)-(I) have been withdrawn, and therefore, nucleotide sequences encoding SEQ ID NO: 4-12 will be examined together.

Applicant's arguments regarding the restriction between the invention of Group I and II are not deemed persuasive for the following reasons: the invention of Group I is directed to nucleotide sequences which are not required by the invention of Group II. Also, the method of removing ions from a source of Group II differs from the method of producing recombinant chelons of Group I in starting material, end products, and method steps. In addition, since the literature search of the two groups is highly divergent, their coexamination will pose search burden upon the Examiner. Therefore, the restriction requirement between invention of Groups I and II is proper.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-9 are under examination. Claims 10-16 are withdrawn from consideration as being directed to a non-elected invention.

Drawings

The drawings filed 05/09/02 are approved by the Examiner.

Claim Objections

In claims 1-3, it is suggested that "a sequence" be changed to ---a nucleotide sequence---.

In claim 3, "as well as" should be replaced with ---and---.

In claims 5-6, it is suggested that "to contain" be changed to -- with--.

In claim 7, "which is" before "comprises" should be deleted.

In claim 8, it is suggested that "wherein the chelon protein which is encoded" be changed to ---wherein the encoded chelon protein----.

In claim 9, it is suggested that ---protein--- is inserted after "chelon", in step (b), for clarification.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 9 is indefinite in the recitation of "infecting. .....with a vector". The specification does not define "infecting", and therefore, the term is open to an individual interpretation. In addition, the terms "infecting" and "transforming" are not interchangeable, as recited in the claim. Therefore, the recitation "infecting or transforming" renders the claim indefinite.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 3, 5-6 and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA recombinant molecule comprising an isolated nucleotide sequence encoding the synthetic proteins comprising the amino sequence of SEQ ID NO: 4-12 that binds mercuric ions and a host cell

transformed with said DNA molecule and a method of recombinantly producing said proteins, does not reasonably provide enablement for a DNA recombinant molecule comprising a sequence encoding any chelon protein that binds mercuric ions and a host cell transformed with said DNA molecule. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to a non-naturally occurring recombinant DNA molecule comprising a sequence encoding any chelon protein that binds to mercuric ions and a host cell transformed with said recombinant DNA. Claim 9 is drawn to a method for recombinantly producing a chelon protein by infecting a host cell with a vector comprising a promoter operably linked to the disclosed DNA sequence. The specification defines "chelons" as artificial metal binding proteins. The claims encompass any and all DNA sequences encoding artificial proteins that bind mercuric ions.

Applicant provides guidance for the cloning of a coding sequence encoding the chelon protein of SEQ ID NO: 4 from the MerR protein of the Tn21 mer (mercury resistance) operon from the *Shigelli flexneri* INC plasmid R100 (Figure 4). Applicant teaches that MerR protein is a metalloregulatory switch activating transcription of a mercury resistance operon in the presence of mercuric ions. Applicant further teaches that the disclosed chelon protein binds not only to mercury but a variety of metals such as Cd, Co, Cu, Pb and Zn with relatively high affinity and has mercury (Hg) occupancy that is 3 fold higher than that of the wild type MerR protein (Tables 3 and 4). Applicant

further teaches variants SEQ ID NO: 5-12 derived from SEQ ID NO: 4. Applicant teach that SEQ ID NO: 5-12 varies from SEQ ID NO: 4 in one or two amino acid positions and that the sequences are capable of binding cadmium as well as mercury ions with high affinity (Table 2).

Applicant has not taught identification and obtention of nucleotide sequences encoding chelon proteins other than SEQ ID NO: 4-12 of *Shield flexneri.* On page 1, line 15 of the specification, Applicant states "(o)ne of the best-characterized mercury resistance (mer) operons is located on transposon Tn21 from the *Shigelli flexneri* INcFII plasmid R100". However, Applicant has not taught other best -characterized mer operons which would allow one skilled in the art to obtain chelon-encoding sequences as broadly claimed. The state of the prior art teaches that the mer locus occurs on gram negative and gram-positive bacterial plasmids or on the chromosome, and that the best-characterized examples of mer are on the gram-negative transposons Tn21 and Tn 501 (Ross et al. Journal of Bacterial, 1989). The instant claims are not limited to nucleotide sequences encoding chelons from Tn21 and Tn501. The claims encompass any and all DNA sequences encoding artificial proteins that bind mercuric ions. To claim nucleotide sequences encoding any and all chelons that bind mercuric ions without specific guidance for how to identify and obtain their specific natural sources and analysis of their transcriptional regulation is an invitation to experiment requiring undue experimentation. Claim 9 is rejected because Applicant has not provided guidance for a method of "infecting" a host cell with the chelon encoding DNA sequence to produce a recombinant chelon protein. The state of the prior art does not teach that infecting a

host cell with a DNA will result in a recombinant protein. Therefore, without guidance on infecting a host with a DNA to produce a recombinant protein, one skilled in the art is left with trial and error experimentation considered undue.

Therefore, given the breadth of the claims, the lack of sufficient guidance as discussed above, the state of the prior art, the claimed invention is not enabled throughout the broad scope.

Written Description

Claims 1, 3 and 5-6 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a non-naturally occurring recombinant DNA comprising nucleotide sequences encoding all chelon proteins that bind to mercuric ions and cadmium, a host cell transformed with said recombinant DNA molecule.

Applicant describes synthetic nucleotide sequences encoding proteins of SEQ ID NO: 4-12 that bind heavy metal ions and a host cell transformed with said nucleotide sequences. Applicant has not described all "artificial mercury binding proteins" other than SEQ ID NO: 4-12. These are genus claims.

See, *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997) where it states "A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to

members of the genus, which features constitute a substantial portion of the genus. See also where the court teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from the organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism. See, also Written description Examination Guidelines published in Federal Registry/Vol. 66, No.4/Friday, January 5, 2001/Notices).

Applicant has not described nucleotide sequences encoding chelon proteins other SEQ ID NO: 4-12 of Shield flexneri. While the state of the prior art describes the MerR protein from Tn21, other MerR proteins that bind to mercuric ions encompassed by the claims are not described. Applicant has not described structural elements/feature common to all chelon encoding sequences, which would allow one to predictably determine what will be the identity of the non-disclosed sequences. Since Applicant has not described the nucleotide sequences as broadly claimed, host cells comprising said nucleotide sequences are similarly not described. Therefore, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that Applicants were in possession of the claimed invention.

Remarks

Claims 1-9 are free of the prior art of record because the prior art does not teach or suggest isolated nucleic acids that encode SEQ ID NO: 4-12.

Claim 4 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Papers related to this application may be submitted to Technology Sector 1 by facsimile transmission. Papers should be faxed to Crystal Mall 1, Art Unit 1638, using fax number (703) 308-4242. All Technology Sector 1 fax machines are available to receive transmission 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Medina A. Ibrahim whose telephone number is (703) 306-5822. The Examiner can normally be reached Monday-Thursday from 8:30AM to 5:30PM and every other Friday 9:00AM to 5:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Amy Nelson, can be reached at (703) 306-3218.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

6/10/03
Mai

Amy Nelson

AMY J. NELSON, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600